REMARKS

Claims 1-12 are pending in the present application, with claims 1 and 7 being the independent claims.

Rejection under 35 U.S.C. §112, first paragraph

On page 2 of the April 26, 2004 Office Action, claims 1-12 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

The Examiner stated that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner also stated that this is a new matter rejection.

The Examiner stated that claim 1 and 7 have been substantively amended. The Examiner also stated that the Applicant has not pointed to any basis for these changes and none is apparent. The Examiner further stated that it is noted that the present form of claims 1-12 bears limited resemblance to original claims 1-12.

The Examiner stated that Applicant must point out by page and line number the basis for each step (individually and as being part of the recited process steps collectively) in support of the system and process as now claimed. The Examiner also stated that the limitation set forth in the instant claims do not match those of the original claims in a broad sense or in particulars. The Examiner further stated that failure to point to basis in applicant's next response will be considered non-responsive.

In response, Applicants respectfully traverse the rejection.

Applicants maintain that the patent specification demonstrates that Applicants had possession of the claimed invention at the time the application was filed.

Applicants submit herewith as **Exhibit A** attached hereto a chart citing exemplary support in the application as filed, for each element in the claims. As shown in Exhibit A, each claim element is adequately supported in the specification.

The chart cites portions of page 10, line 29 through page 12, line 4 ("the cited passage") of the specification as exemplary support for several elements of the process claims (7-12). It should be noted that the cited passage sets forth an exemplary embodiment, and moreover it expressly states that the elements contained therein **may** be included in the described process. Thus, one skilled in the art would understand that one can pick and choose from amongst the elements contained in the cited passage to practice the claimed invention of this application, unless the application states elsewhere that a particular element must be included.

The Office Action appears to imply that the rejection is based on lack of verbatim support in the specification for the claim elements.

Although some of the elements in the pending claims are not a verbatim copy of a corresponding element in the cited passage, the Office Action does not cite to any particular patent law, patent rule or other legal authority having binding force which requires verbatim support in the specification for a patent claim. Indeed, it is submitted that it is generally the accepted

practice before the PTO that the support in the specification for a claim element need not be a verbatim copy of the claim element.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-12 under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §112, first paragraph

On page 3 of the April 26, 2004 Office Action, claims 1-12 were rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for some aspects of the claimed method and system, purportedly does not reasonably provide enablement for the breadth of what is encompassed.

The Examiner stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Examiner stated that claims 1-6 are directed to a system comprising a database, at least one bioinformatics tool, a protein synthesis means having a screening means, a protein processing means, a crystallization means, an X-ray crystallography means, a structure extraction means, and a homology model building tool. The Examiner also stated that the prior Office Action sets forth the reasons that an integrated, turn-key system or fully automated system is not enabled. The Examiner further stated that Applicant's response essentially concedes that such a system is not enabled and argues that the unintegrated system is enabled and claims 1-6 embrace an integrated system that is not enabled.

The Examiner stated that the system of claims 1-6 encompasses a synchrotron. The Examiner also stated that the prior Office Action sets forth the reasons that a system including this apparatus as well as a method using this apparatus are not enabled. The Examiner further stated that Applicant argues on page 13 of the response that a number of publicly accessible facilities that include synchrotrons with undulator beams exist. The Examiner stated that this is not agreed with. The Examiner also stated that the beamline time must be applied for at existing synchrotron facilities. The Examiner further stated that many requests for use are turned down due to lack of facilities. The Examiner stated that Applicant has not established that synchrotrons would have been readily available and accessible to those wishing to practice the claimed invention. The Examiner also stated that while applicant argues there is no bar against the patenting of inventions that are costly to practice, the Examiner maintains that as set forth in the prior Office Action, synchrotrons cost approximately $100,000,000.00, take approximately 10 years to build, and can't be purchased from a catalog. The Examiner further stated that this is not so much costly as prohibitive to those wishing to practice the invention. To the best of the Examiner's knowledge, the inventors themselves are not in possession of a synchrotron but must also arrange to use existing facilities to practice the claimed method.

The Examiner stated that with respect to claims 7-12, the claimed method fails to particularly point out what steps are to be performed and how they are to be performed. The Examiner also stated that for example, claim 7 recites "using at least one bioinformatics tool and the sequence information, structural information and functional information stored in the database."

The Examiner further stated that this does not illuminate which bioinformatics tool, what specific information, or how to use it to achieve the goal of clustering.

The Examiner stated that it does not provide the positive, active steps to perform on unspecified structural or sequence information to arrive at a plurality of families within the context of the claims. The Examiner also stated that for example, the database has sequence information for a first plurality of proteins and structural information and functional information for a second plurality of proteins. The Examiner further stated that for example, say the structural information for the second plurality is polymeric structure (monomer, dimer, etc.).

The Examiner stated that for example, say the functional information for the second plurality is enzymatic activity (protease, synthase, etc.) how does one practicing the invention use polymeric structure and enzymatic activity to cluster into a plurality of families. The Examiner also stated that for example, proteins A, B and C are in the first plurality and proteins D, E and F are in the second plurality. The Examiner further stated that protein D is a monomeric protease, protein E is a trimeric synthase and protein F is a monomeric protease.

The Examiner questions what is the plurality of families that the at least one bioinformatics tool identifies. The Examiner also questions how are homologous sequences for the family determined if the database does not contain sequence information for D, E and F and their sequences cannot be compared to sequence information for A, B and C. The Examiner stated that the specification provides no discussion or guidance for adapting

bioinformatics tools to make such determinations. The Examiner also stated that going further in the claim to step (g), the refined model is stored in the database. The Examiner further stated that part (a) does not require that the structural information include a refined model or a homology model.

The Examiner stated that going further in the claim to step (j), the database is updated to link the refined model to other databases. The Examiner also stated that part (a) does not require that the database have links to any information at all. The Examiner further stated that the method steps as written are internally inconsistent and as written, one of ordinary skill in the art would be unable to practice the method for at least these reasons.

In response, Applicants respectfully traverse the rejection.

Regarding "integrated system", the Office Action appears to imply that system claims in general can only be directed to integrated systems. However, Applicants know of no legal authority which supports such a premise, and no such authority has been cited.

In addition, the Office Action has not specified what are the requirements for a system to be "integrated."

On the other hand, Fig. 1 of this application shows a system in which database 1 is a central repository for information and data which is connected to the other components in the system and can funnel the stored data and information to the other components. Accordingly, Applicants disagree with the contention that the specification does not enable an integrated system.

Regarding the availability of a synchrotron, the Office Action appears to imply that the enablement requirement is met only if one can own each and every component of a claimed invention and that the test of possession is ownership. Again, Applicants know of no legal authority which supports such premise, and no such authority has been cited.

Applicants maintain that ownership cannot be the test for possession. For example, one can possess a car obtained through a lease. The lessee clearly can operate it and use it for any lawful purpose.

The Office Action entirely rejects the notion of leasing time on a synchrotron in order to practice the claimed invention, simply based on the assumption that many requests for access to a synchrotron are rejected.

Again, returning to the example of leasing, many applicants for automobile leases are rejected, for one reason or another. Yet, others can readily possess an automobile through a lease without any problems.

Similarly, beamtime can readily be leased by general users. See, for example, http://www.aps.anl.gov/aps/frame_beamtime.html, regarding leasing beamtime on the APS beamline. The APS is just one example of a beamline facility which openly advertises beamtime leasing by non-owners who submit applications.

In addition, it should be noted that the test for whether a synchrotron is available for practicing the claimed invention is not whether any person coming off the street can obtain time on a synchrotron for any non-specific purpose.

Regarding claims 7-12, the Office Action states that the claims do not recite sufficient, specific acts in connection with clustering proteins into families, using a bioinformatics tool and information stored in the database. Applicants know of no legal authority which imposes such requirement, and no such authority has been cited.

It should be noted that while Applicants maintain that the clustering step itself is recitation of an act to be performed, the law does not require that each step must include one or more acts. See, for example, 35 U.S.C. §112, sixth paragraph, which specifically provides for the recitation of step-plus-function elements without recitation of any acts in support thereof, which would nevertheless be construed to cover the corresponding acts described in the specification (and equivalents).

In addition, the rejection of the process claims is premised on the contention that the claims do not provide sufficient details to teach one how to practice the claimed invention.

However, it is not the purpose of patent claims to teach one how to practice the claimed invention. It is well-established by relevant Federal Circuit case law, as well as other relevant guidelines, that one looks to the specification, and not to the claims, for guidance regarding how to practice the claimed invention. See, for example, S3 Inc. v. Nvidia Corp., 259 F.3d 1364, 1369 (Fed.Cir. 2001). See also MPEP §2164.08 which states that one "does not look to the claims but to the specification to find out how to practice the claimed invention."

The specification clearly explains (see, for example, page 14,

lines 18-26) that readily available bioinformatics tools such as BLAST can be used for the clustering step.

Regarding the various hypotheticals posed in the Office Action, it is noted that an applicant need not specify or predict every possible problem or issue that can be encountered during practice of the claimed invention. Moreover, a patent claim does not need to recite provisions for overcoming such problems or issues. A claimed invention merely needs to be useful. There is no legal requirement that a claimed invention has to overcome all problems before it can be patented.

Regarding the addition of information to the database organized in step (a) of claim 7, the application clearly teaches that information and data are added to the database as they are obtained in the process. There is no requirement in the application that all information and data to be added to the database must be initially organized in the database before the process can proceed to the subsequent steps.

Applicants maintain that the application provides an enabling disclosure for each and every feature of the claimed invention.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-12 under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

On page 5 of the April 26, 2004 Office Action, claims 1-12 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention.

The Examiner stated that "claims 1 and 7 recite 'homologous sequences.'". The Examiner further stated that "it is unclear what level of homology is required to meet the limitation of the claim."

The Examiner stated that claims 1 and 7 recite 'a plurality of target proteins which are members of the family.' The Examiner also stated that "the criteria that define a family are not provided." The Examiner further stated that "it is unclear how a target is selected (what parameters or criteria are used) and how many targets are selected."

The Examiner stated that Applicant argues that various know programs can be used and that one of ordinary skill in the art would not find these two phrases unambiguous and this is unpersuasive. The Examiner also stated that the claims and specification must particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner further stated that Applicant has not provided an art understood meaning for these phrases either within the specification or using art recognized documentation.

The Examiner stated that claims 1 and 7 have been amended to recite "which are effective as the target proteins." The Examiner also stated that it is not known what is meant by this phrase. The Examiner further stated that what defines an effective target protein.

The Examiner stated that claims 1 and 7 have been amended to recite "screening products of the synthesis to choose selected

synthesized products for processing." The Examiner further stated that "the criteria or parameters for the selection are not provided."

The Examiner stated with respect to claims 1-6, the claimed system does not set forth the relationship of the database, bioinformatics tool, protein synthesis means, protein processing means, crystallization means, X-ray crystallography means, and so forth. The Examiner also stated that the claim language does not reflect an integrated or turn-key system where the components are related or linked to each other in some fashion. The Examiner further stated that as written, the claim appears to be directed to a collection of laboratory equipment or machines.

The Examiner stated that a collection of laboratory equipment or machines does not define a system. The Examiner also stated that Applicant's response on page 18 indicates that the claim is not limited to a turn-key system.

The Examiner stated that with respect to claims 7-12, the method steps as written are internally inconsistent and unclear. The Examiner also stated that for example, in step (a) the database has sequence information for a first plurality of proteins and structural information and function information for a second plurality of proteins. The Examiner further stated that in step (g), the refined model is stored in the database.

The Examiner stated that part (a) does not require that the structural information include a refined model or a homology model. The Examiner also stated that in step (j), the database is updated to link the refined model to other databases. The Examiner further stated that part (a) does not require that the

database have links to any information at all.

Applicants traverse the rejection as follows.

Regarding level of homology and criteria for a family, the application provides, for example, the following additional guidance at page 14, lines 3-16: "Three dimensional structural information may be exploited in conjunction with recent advances in amino acid sequence analysis to construct the database. Advanced bioinformatics tools 2 are used to cluster all known gene products into families of homologous sequences. The clustered gene products are typically similar at approximately 30% identity, <0.001 probability of error. The structure of a representative member for each and every family is determined. The protein classes may include whole proteins, domains or sequence motifs that may or may not correspond to independent modules. The unsolved members, which probably constitute the majority, of each family may be visualized by homology modeling based on the known structures of family representatives, as described below."

Regarding products of synthesis which are effective as the target proteins and screening such products, it is submitted that it is well known to one skilled in the art that processes for synthesizing proteins, such as through cloning, generally do not have 100% yield, that is, some of the products of the synthesis are not effective as the target proteins (for example, are not proteins at all, have the structure of another macromolecule, etc.). Methodologies for screening the products of synthesis for products which are effective as the target proteins are generally well known, and may vary according to the target protein, as known to one skilled in the art. See, for example, the *Lima*

(1997) paper [a copy of which was submitted with Applicants' October 19, 1999 Information Disclosure Statement] identified in the application at page 25, lines 34-37 as an example of the state of the art at the time this application was filed.

With respect to system claims 1-6, as discussed above, no authority has been cited in support of the premise in the Office Action that system claims have to be directed at integrated or turn-key systems.

Contrary to the Office Action, the elements of claims 1-6 are related or linked to each other. As mentioned above, the database described in claim 1 is a central repository for information and data (for a plurality of proteins) and can funnel the stored data and information to the other components. For example, the bioinformatics tool uses the information stored in the database to cluster the proteins. The protein synthesis means synthesizes target proteins using information stored in the database. The X-ray crystallography means performs high-throughput crystallography, and includes analyzing means for analyzing diffraction data, means for building an atomic model according to an analysis of the diffraction data, means for refining the model and storing the refined model in the database. The structure extraction means analyzes the refined model using information stored in the database. The homology model building tool use the refined model retrieved from the database to develop a homology model for predicted protein structures. The homology model is used to update the database to link the refined model to other databases.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-12 under 35

U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. §102(a)

On page 7 of the April 26, 2004 Office Action, claims 1-12 were rejected under 35 U.S.C. §102(a) as allegedly anticipated by knowledge of others in this country before the invention thereof by Applicant, as purportedly evidenced by the Workshop on Structural Genomics held at Argonne National Laboratories held January 1998, Nation Institute of General Medical Sciences (NIGMS) Protein Structure Initiative (PSI) held April 24, 1998 (hereinafter "the NIGMS PSI paper"), NIGMS Genomics Project Planning Meeting held November 24, 1998, Structural Genomics Meeting held October 1998 in Avalon, New Jersey, Shapiro et al. (Current Biology, 15 March 1998) and Gaasterland (Nature Biotechnology, July 1998).

The Examiner stated that the prior Office Action rejected claim 1-12 under 102(a) as being anticipated by the National Institute of General Medical Sciences (NIGMS) Protein Structure Initiative (PSI) Meeting Summary dated April 24, 1998 (hereinafter "the NIGMS PSI paper"). The Examiner also stated that the NIGMS PSI paper "summarized the discussion of a one-day meeting held on April 24, 1998 to experimentally determine 3D structures of protein families via a representative protein molecule (target) from each family."

The Examiner stated that "protein sequences were compared using sequence homology to define families and targets selected." The Examiner also stated that "the targets are then cloned into plasmids for overexpression, and purified for use in crystallization trials." The Examiner further stated "those targets successfully crystallized have X-ray crystallography and

protein structure determination performed."

The Examiner stated that "synchrotrons, multiwavelength anomalous diffraction (MAD), and selenomethionyl enrichment are specifically disclosed." The Examiner also stated that "structural and functional properties would be predicted." The Examiner further stated that "in particular, identification of protein fold motifs is disclosed."

The Examiner stated that "the results of the analysis are put in a database with any additional information that may be helpful for further experiments." The Examiner also stated that "the database is updated and annotated as research progresses." The Examiner further stated that "the database is intended to be accessible to all researchers."

The Examiner stated that "implicit in this document is a system containing the component parts (database and means) for executing each of the steps of the method."

The Examiner stated that Applicant submitted the Teng Declaration and argues that this publication is not prior art. The Examiner also stated that it is noted that applicant concedes an availability date of May 12, 1999 for this material as a publication. The Examiner further stated that Applicant argues that the content of any prior version cannot be verified.

The Examiner stated that Applicant is advised that Exhibits 2 and 3 of the Teng Declaration appear to be identical. The Examiner also stated that neither exhibits list the modification dates referred to in Exhibit 1 and further clarification is requested.

The Examiner stated that 35 USC 102(a) is not limited to description in a printed publication before the invention thereof by the applicant for patent. The Examiner also stated that it includes whether the invention was known by others in this country before the invention thereof by the applicant for a patent. The Examiner further stated that the fact that this meeting (as well as the other meeting cited above and publication discussing the meetings cited above) took place or were published prior to applicant's filing date indicates that the invention was known.

The Examiner stated that Applicant has not presented evidence disputing the content of what was discussed at these meetings. The Examiner also stated that Applicant has submitted Exhibits 1-10 on September 30, 2002. The Examiner further stated that the draft agenda, letters, slides from oral presentations, Hendrickson's notes, etc. are all consistent with the meeting summaries.

The Examiner stated that in particular, Hendrickson's notes from Chris Sander's talk include comments on homology modeling, deriving families, and picking a 3D target from each family. The Examiner also stated that his notes from Paul Godowski's talk include comments on going from cDNA to crude protein to pure protein to crystals (including assaying for quality crystals) to structure. The Examiner further stated that his notes from Janet Thornton's talk include comments about basic data, family sequence and structure information, functional motifs in 3D, ligand binding sites and linking this information to functional information, pathway information, expression and genome data.

The Examiner stated that the summary of the NIGMS SGPPM dated

November 24, 1998 indicates that the various experimental components of the structural genomics project were summarized, especially the high-throughput method. The Examiner also stated that the computational tasks of protein classification and target selection under way in various laboratories was discussed. The Examiner further stated that the expected benefits were discussed.

The Examiner stated that Shapiro et al. also summarizes the Argonne Structural Genomics Workshop in a meeting review. The Examiner also stated that the goal of building a comprehensive structural database using large-scale structure determination X-ray crystallography (including crystal freezing and MAD phasing and third generation synchrotrons having undulator beamlines) is disclosed. The Examiner further stated that a class based approach using sequences and determination of the structure of a representative number from each and every class is disclosed.

The Examiner stated that as set forth in the prior Office Action "Gaasterland reviews the goals and initial results of the structural genomics initiative." The Examiner also stated that "results from the pilot project presented in January 1998 at the Argonne National Laboratory are discussed." The Examiner further stated that "flow diagrams (Figures 1 and 2) and particular bioinformatics tools (Table 1) with the accompanying discussion are considered to disclose the claimed methods and systems."

The Examiner stated that Gaasterland discloses genome analysis and target selection. The Examiner also stated that the genome information disclosed is clearly in the context of an annotated sequence database. The Examiner further stated that cross-genome comparisons would clearly indicate clustering and homologous

sequence analysis to one of ordinary skill in the art, particularly where selection of targets is discussed.

The Examiner stated that it is noted that Gaasterland specifically discusses the Protein Data Bank (PDB) which would have been known at the time of the invention to contain information including atomic coordinates, bibliographic citations, primary and secondary structure information, crystallization structure factors. The Examiner also stated that this includes pointers to other databases which contain a variety of additional information. The Examiner further stated that the PDB would have bee internet accessible.

The Examiner stated that with respect to the system of claims 1-6, applicant has conceded that the named components are not required to be linked in any particular fashion as a turn-key system. The Examiner also stated that these claims do not require that the output from means must be in a form to act directly, automatically, seamlessly, or otherwise, as input for the next means. The Examiner further stated that each of these discrete components (a database with sequence, structural, and functional information; at least one bioinformatics tool capable of clustering; protein synthesis means with screening means; protein processing means; crystallization means; X-ray crystallography means; structure extraction means able to build a refined model; and a homology building tool) having the functionality required by the claims, would have been discussed at these various meetings and thus the system as claimed would have been known.

The Examiner stated that the documents of record pertaining to the cited meetings provide every indication that the claimed

system and method were discussed in a general way and a particular way with respect to particular methodologies to practice the method to those in attendance. The Examiner also stated that the structural genomics problem was the whole point of these meetings. The Examiner further stated that the flow chart of Gaasterland and knowledge of skill in the art on the various techniques would have enabled one to practice the invention.

The Examiner stated that should applicant argue otherwise, they are inviting an enablement rejection with respect to their methods for the same reasons. The Examiner also stated that it is noted that Gaasterland was both an organizer and a presenter at the January meeting.

As an initial note, the rejection is based on three separate cited references. It is well-established that anticipation under 35 U.S.C. §102 requires that each and every feature of a claimed invention must be disclosed in a single reference.

Here, (i) the NIGMS PSI paper, (ii) the NIGMS Genomics Project Planning Meeting held November 24, 1998, (iii) Structural Genomics Meeting held October 1998 in Avalon, New Jersey, (iv) Shapiro and (v) Gaasterland are clearly separate and distinct references. Accordingly, a rejection under 35 U.S.C. §102(a) based on a combination of these references is improper and should be withdrawn.

None of the references predates Applicants' invention and discloses each and every element of the claimed invention.

For example, the NIGMS PSI paper appears to be a computer

printout, made on October 12, 2001, of selected web pages at the web site of the NIGMS.

Applicants have sought the archival records of the source of the NIGMS PSI paper, as evidenced in the Teng Declaration. According to Exhibit 1 to the Teng Declaration which is an e-mail message received by the declarant from the custodian of the archival records, the records do not indicate that the NIGMS PSI paper was available prior to May 12, 1999. The e-mail message states that two electronic files are attached thereto. The e-mail message further states that the first electronic file (Exhibit 2 attached to the Teng Declaration) corresponds to the current NIGMS web page (hereinafter "the current NIGMS PSI web page file"), at the web address http://www.nigms.nih.gov/news/reports/protein_structure.html, on which the NIGMS PSI paper is displayed. The e-mail message also states that the other electronic file (Exhibit 3 attached to the Teng Declaration) corresponds to the previous version of the NIGMS web page (hereinafter "the previous NIGMS PSI web page file") on which the NIGMS PSI paper was displayed. The e-mail message further states that (a) the current NIGMS PSI web page file (i.e. Exhibit 2) was last modified March 8, 2000, and (b) the previous NIGMS PSI web page file (i.e. Exhibit 3) was last modified May 12, 1999. Further, the e-mail states that no other versions of the NIGMS web page on which the NIGMS PSI paper is displayed were found at NIGMS.

Therefore, the reference apparently post-dates this application's filing date.

Although the text of the NIGMS PSI paper purports that it is a report of a meeting on April 24, 1998 and that the document was

updated on June 2, 1998, Applicants submit that the date information in the text of the electronic files is less reliable than the information of creation and modification dates, maintained by the computer operating system which archives the relevant electronic files (i.e. corresponding to Exhibits 2 and 3, respectively). Here, as indicated in the e-mail from Mr. Hogan, the dates of last modification of the electronic files corresponding to Exhibits 2 and 3, respectively, are March 8, 2000 and May 12, 1999. No evidence has been obtained or presented that the content of the electronic files was disseminated and publicly available prior to May 12, 1999.

Accordingly, the earliest date that can be attributed to the NIGMS PSI paper is May 12, 1999. The subject application was filed January 22, 1999. Since it has not been shown that the NIGMS PSI paper was disseminated and publicly available prior to the January 22, 1999 filing date of the subject application, Applicants maintain that the NIGMS PSI paper is not prior art to the invention claimed in the subject application.

In addition, Applicants maintain that it has not been demonstrated that the NIGMS PSI paper is an accurate record of the discussion at the April 24, 1998 NIGMS PSI meeting. Since the earliest date which can reliably be attributed to the web page files corresponding to the NIGMS PSI paper at this time is May 12, 1999 (i.e. more than one year after the meeting), the NIGMS PSI paper is no more reliable for what it purports to report than other hearsay materials which are traditionally deemed to be unreliable because, amongst other reasons, the hearsay material was not generated contemporaneously with the events which it purports to summarize. Hearsay material such as the NIGMS PSI paper is also unreliable because it represents the

recollection of the author which, such as here, may be faulty for a number of reasons and cannot be tested. Indeed, here the author of the NIGMS PSI paper is not even known.

Although the NIGMS PSI paper may be said to represent knowledge (of someone) as of May 12, 1999, it has not been demonstrated that it reliably reports the discussion at the April 24, 1998 NIGMS PSI meeting. Therefore, Applicants maintain that the NIGMS PSI paper is not evidence of knowledge of others at the time of the April 24, 1998 NIGMS PSI meeting.

Applicants also maintain that it has not been shown that the NIGMS PSI paper is more than the knowledge of the author thereof after the filing of this application. Therefore, it is submitted that the NIGMS PSI paper does not render the claims unpatentable under 35 U.S.C. §102(a).

The Gaasterland paper does not disclose or suggest the claimed invention.

The Gaasterland paper is a survey of assorted independent research being conducted at the time of the survey.

The Gaasterland paper does not provide an enabling disclosure of, and therefore cannot anticipate, the claimed invention.

For example, the Gaasterland paper mentions a number of independent research projects which were being conducted by assorted individuals. Figure 1 of the Gaasterland paper shows a high level flow chart. No specifics are provided by the Gaasterland paper regarding how each element of the chart would tie together with the other elements in the chart, and the

textual content of the Gaasterland paper does not provide the details of the step purported represented by the element. Figure 2 is a high level graphical representation of a protein database (PDB) and contents thereof. Figure 2 (a) does not tie each element of Figure 1 together with the other elements in Figure 1, and (b) does not provide the details of the step purported represented by the element in Figure 1.

Figures 1 and 2 and the textual content of the Gaasterland paper cannot constitute an enabling disclosure of, and therefore cannot anticipate, the claimed invention.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-12 under 35 U.S.C. §102(a).

Rejection under 35 U.S.C. §102(f)

On page 11 of the April 26, 2004 Office Action, claims 1-12 were rejected under 35 U.S.C. §102(f) because the applicant purportedly did not invent the claimed subject matter in view of the Workshop on Structural Genomics held at Argonne National Laboratories held January 1998, NIGMS PSI paper, NIGMS Genomics Project Planning Meeting held November 24, 1998, Structural Genomics Meeting held October 1998 in Avalon, New Jersey and Gaasterland.

The Examiner stated that while at least inventor Hendrickson is indicated to have been present at some of the meetings, the claimed invention in its totality appears to have been conceived of by a multiplicity of people and not just Hendrickson and Honig.

As discussed above, none of the cited references anticipates the claimed invention, that is, discloses each and every element of the claimed invention prior to the invention made by Applicants.

The Office Action appears to base the §102 rejections on the collection of knowledge in the minds of a plurality of individuals at various times. As discussed above, such a pool of knowledge does not constitute the required single reference under 35 U.S.C. §102. Nor does the knowledge of each and every element of the claimed invention (the presence of which has not been established by the Office Action) in the pool constitute anticipation under 35 U.S.C. §102.

The Office Action simply has not demonstrated that the claimed invention was known or made by another (i.e. a single reference) prior to when the invention was made by Applicants.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-12 under 35 U.S.C. §102(f).

In view of the remarks hereinabove, Applicants maintain that claims 1-12 are now in condition for allowance. Accordingly, Applicants earnestly solicit the allowance of claims 1-12.

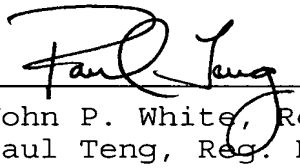
If a telephone interview would be of assistance in advancing prosecution of the present application, Applicants' undersigned attorney invites the Examiner to telephone him at the telephone number provided below.

If a petition for an extension of time is required to make this response timely, this paper should be considered to be such a

petition, and the Commissioner is authorized to charge the requisite fees to our Deposit Account No. 03-3125.

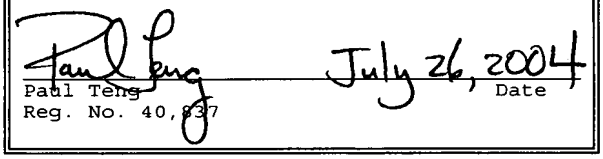
No fee is deemed necessary in connection with the filing of this response. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White, Reg.No. 28,678
Paul Teng, Reg. No. 40,837
Attorneys for Applicants
Cooper & Dunham, LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



July 26, 2004
Date

Paul Teng
Reg. No. 40,837

Pending Claims	**Exemplary Support**
1. A system for determining experimentally a plurality of three-dimensional atomic structures, each of which is associated with a corresponding protein, comprising:	Fig. 1
a database of sequence information for a first plurality of proteins, and structural information and functional information for a second plurality of proteins;	database 1a; 12:35[1] - 13:29
at least one bioinformatics tool adapted to use the sequence information, structural information and functional information stored in the database to cluster the first plurality of proteins into a plurality of families, in which, for each family, members of the family have homologous sequences;	bioinformatics tools 2; 14:3-32
protein synthesis means for synthesizing for each family determined by the at least one bioinformatics tool a plurality of target proteins which are members of the family, using information stored in the database corresponding to the target proteins, the protein synthesis means having	protein synthesis apparatus 3; 15:3-26
screening means for screening products of the synthesis to choose selected synthesized products, which are effective as the target proteins, for processing;	screening apparatus 4; 15:28-32
protein processing means for preparing, purifying and characterizing each of the selected synthesized products screened through the screening means;	protein processing apparatus 5; 15:34 - 16:18

[1] The notation pp:qq denotes reference to the specification, page pp, line qq.

Pending Claims	Exemplary Support
crystallization means for crystallizing the processed synthesized product processed by the protein processing means, to produce a plurality of specimen crystals of the target protein, and testing the plurality of specimen crystals for predetermined diffraction characteristics to determine the specimen crystals which are suitable for diffraction measurement;	crystallization apparatus 6; 16:20-27
X-ray crystallography means for performing high-throughput crystallography on the specimen crystals determined by the crystallization means to be suitable for diffraction measurement, the X-ray crystallography means having diffraction measuring means for measuring for diffraction data the suitable specimen crystals of the target protein, analyzing means for analyzing the diffraction data, means for building an atomic model of the target protein according to an analysis of the diffraction data by the analyzing means, and means for refining the model of the target protein against the diffraction data and storing the refined model in the database;	X-ray crystallography apparatus 8; 16:34 - 20:20
structure extraction means having means for analyzing the refined model of the target protein using sequence information corresponding to other family members which is stored in the database and structural information corresponding to other proteins which is stored in the database, and means for analyzing the refined model for functional motifs and for surface characteristics; and	structure extraction apparatus 9; 20:22-33
a homology model building tool adapted to use the refined model of the target protein retrieved from the database to develop a homology model of one or more predicted protein structures,	homology model building tools 10; 20:35-21:23

Pending Claims	Exemplary Support
wherein the database is updated using the at least one bioinformatics tool and the developed homology model to link the refined model of the target protein to other databases which store information concerning biological pathways and functional annotation.	21:34-36; 22:4-17; 13:34 - 14:1
2. A system according to claim 1, further comprising: cryoprotection means for freezing the suitable specimen crystals, wherein the suitable specimen crystals are frozen by the cryoprotection means before being measured for diffraction data by the diffraction measuring means.	cryoprotection apparatus 7; 16:29-32
3. A system according to claim 1, wherein the protein synthesis means includes cloning means for cloning for each family determined by the at least one bioinformatics tool, in parallel, cDNAs corresponding to the appropriately representative family members into a plurality of expression vectors for a plurality of expressions systems,	15:3-20
the screening means screens for expression constructs obtained by the cloning means to determine ones that are effective as proteins, and	15:28-32
the protein processing means processes the expressed proteins determined to be effective by the screening means.	15:34-35
4. A system according to claim 1, wherein the X-ray crystallography means includes a synchrotron storage ring having undulator beamlines for high-throughput crystallography by a multiwavelength anomalous diffraction method, and	16:34 - 17:1; 17:20-29

Pending Claims	Exemplary Support
the analyzing means analyzes the diffraction data by a multiwavelength anomalous diffraction phasing method.	17:26-27
5. A system according to claim 4, wherein selenomethionine is incorporated in the synthesized target proteins by the protein synthesis means, and the analyzing means using the multiwavelength anomalous diffraction phasing method analyzes diffraction data corresponding to selenomethionyl proteins.	17:9-13
6. A system according to claim 1, wherein the homology model developed by the homology model building tool is used in at least one of target selection, drug design, and design of constructs for experimental analysis.	21:9-12
7. A process for determining experimentally a plurality of three-dimensional atomic structures, each of which is associated with a corresponding protein, comprising the steps of:	10:29-12:4
(a) systematically organizing sequence information for a first plurality of proteins, and structural information and functional information for a second plurality of proteins into a database;	10:32-37; 12:35 - 13:29
(b) clustering the plurality of proteins into a plurality of families, in which, for each family, members of the family have homologous sequences, using at least one bioinformatics tool and the sequence information, structural information and functional information stored in the database;	11:1-3; 14:3-26

Pending Claims	Exemplary Support
(c) synthesizing for each family determined in step (b) a plurality of target proteins which are members of the family, using information stored in the database corresponding to the plurality of target proteins, and screening products of the synthesis to choose selected synthesized products, which are effective as the target proteins, for processing;	11:4-9; 15:3-26
(d) preparing, purifying and characterizing each synthesized product that is chosen in step (c);	11:10-11; 15:34 - 16:18
(e) crystallizing the processed synthesized product prepared, purified and characterized in step (d) to produce a plurality of specimen crystals of the target protein;	11:12-13; 16:20-23
(f) testing the plurality of specimen crystals grown in step (e) for predetermined diffraction characteristics to determine the specimen crystals which are suitable for diffraction measurement;	11:14-15; 16:23-26
(g) performing high-throughput crystallography, including measuring for diffraction data the specimen crystals determined in step (f) to be suitable for diffraction measurement, building an atomic model of the target protein according to an analysis of the diffraction data, refining the model of the target protein against the diffraction data, and storing the refined model in the database;	11:16-24; 16:34 - 20:20
(h) analyzing the refined model, stored in the database in step (g), of the target protein using sequence information corresponding to other family members which is stored in the database and structural information corresponding to other proteins which is stored in the database, and analyzing the refined model of the target protein for functional motifs and for surface characteristics;	11:25-31; 20:22-33

Pending Claims	Exemplary Support
(i) developing a homology model of one or more predicted protein structures using computational tools for homology model building and the refined model of the target protein retrieved from the database; and	11:35-36; 20:35-21:23
(j) updating the database by using the at least one bioinformatics tool and the developed homology model to link the refined model of the target protein to other databases which store information concerning biological pathways and functional annotation,	21:34-36; 22:4-17; 13:34 - 14:1
wherein steps (f) through (j) are repeated for each of the other target proteins.	22:4-17
8. A process according to claim 7, further comprising the step of: freezing the specimen crystals of the target protein which are determined in step (f) to be suitable, wherein the suitable specimen crystals are frozen before being measured for the diffraction data in step (g).	11:16-20; 16:29-32
9. A process according to claim 7, wherein step (c) includes cloning for each family determined in step (b), in parallel, cDNAs corresponding to the appropriately representative family members into a plurality of expression vectors for a plurality of expressions systems, constructs obtained in the cloning are screened for expression to determine the ones that are effective as proteins, and the expressed proteins determined to be effective are processed in step (d).	11:4-11; 15:3-35

Pending Claims	Exemplary Support
10. A process according to claim 7, wherein the high-throughput crystallography in step (g) is performed using a synchrotron storage ring having undulator beamlines along with a multiwavelength anomalous diffraction method, and the diffraction data measured in step (g) is analyzed using a multiwavelength anomalous diffraction phasing method.	16:34 - 17:1; 17:20-29
11. A process according to claim 10, wherein selenomethionine is incorporated in the plurality of target proteins synthesized in step (c), and the multiwavelength anomalous diffraction phasing method is used to analyze diffraction data measured for selenomethionyl proteins.	17:9-13
12. A process according to claim 7, further comprising the step of using the homology model developed in step (i) in at least one of target selection, drug design, and design of constructs for experimental analysis.	11:37 - 12:2; 21:9-12